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Original article

Clinical characteristics and treatment outcomes of severe (ICU) COVID-19 patients in Saudi Arabia: A single centre study

Saleh Alghamdi

PII: S1319-0164(21)00155-9
DOI: <https://doi.org/10.1016/j.jsps.2021.08.008>
Reference: SPJ 1293

To appear in: *Saudi Pharmaceutical Journal*

Received Date: 26 February 2021
Revised Date: 2 July 2021
Accepted Date: 1 August 2021

Please cite this article as: Alghamdi, S., Clinical characteristics and treatment outcomes of severe (ICU) COVID-19 patients in Saudi Arabia: A single centre study, *Saudi Pharmaceutical Journal* (2021), doi: <https://doi.org/10.1016/j.jsps.2021.08.008>

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Clinical characteristics and treatment outcomes of severe (ICU) COVID-19 patients in Saudi Arabia: A single centre study

Abstract

Background: There is limited information describing the presenting features and treatment outcomes of intensive care unit (ICU) patients with coronavirus disease 2019 (COVID-19) in Saudi Arabia.

Objective: To investigate the clinical, epidemiological, laboratory, radiological, vital signs and treatment characteristics/outcomes of severe (ICU) COVID-19 patients in Albaha region, Saudi Arabia.

Methods: A retrospective cohort study was conducted from 01 April 2020 to 31 August 2020 involving files review of 171 patients admitted to the ICU of a COVID-19 treatment centre as a result of severe symptoms.

Results: Around a third of the ICU patients admitted were over 66 years of age, 59.6% males, 45% diabetics, 39% hypertensive, 25.7% smokers. Patients had symptoms such as 79% fever, 78% cough, 75% headache, 59% sore throat, 57% runny nose, and 75% cough. More than half of the patients had less than 90% oxygen saturation. Bilateral infiltration was present in about 43% of patients. 85.4% lymphopenia, and 70.8% D-dimer (>0.5 u/ml) were the most significant laboratory results. The median stay in the hospital ranged from 4 to 15.6 days, and the ICU time ranged from 4 to 12.7 days. Approximately 29% of patients received antiviral, antimalarial, and antibiotic treatment, while 27.5% of patients received antibiotics and antimalarial therapy alone. Incorporating hydroxychloroquine in treatment protocols did not improve patients' outcomes.

Conclusions: Older age and cardio-metabolic comorbidities increase the risks of severe COVID-19. Different treatment protocols fail to improve mortality rates and urgent efforts are required to prevent the disease and reduce its severity.

Keywords: Coronavirus; COVID-19; antibiotics; hydroxychloroquine; intensive care unit; Saudi Arabia.

1. Introduction

Globally, there are 109,555,318 confirmed cases of COVID-19 as of February 17, 2021, including 2,420,451 deaths (World Health Organization, 2020). The first confirmation case was registered in Saudi Arabia on 2 March 2020. From 2 March to 17 February 2021, there are 373,702 confirmed cases of COVID-19 with 6445 deaths (Saudi Ministry of Health, 2020). Saudi Arabia has a population of 34,218,169 of which 497,068 people live in Albaha region (General Authority for Statistics, 2019).

Due to the different demographics, comorbidities and response of the immune system in the various populations, the seriousness of the disease appears variable. Pneumonia may be the most frequent manifestation of acute respiratory distress syndrome (ARDS). Other serious complications have been reported, including arrhythmia, septic shock, and multi-organ failure (Arentz et al., 2020; Chen et al., 2020). Older persons with comorbidities and polypharmacy

have a higher risk for drugs interactions, side effects, complications and high probability of viral infection (Hammad et al., 2020, 2019b, 2019a, 2017; Mangi et al., 2020).

Although numerous studies reported on the epidemiology and typical presentation of COVID-19 patients in Saudi Arabia (Alsofayan et al., 2020; Alyami et al., 2020; Shabrawishi et al., 2020), regional data is still needed to improve emergency response planning and optimise the use of healthcare resources.

The aim of this study is to investigate the clinical, epidemiological, laboratory, radiological, vital signs and treatment characteristics/outcomes of severe (ICU) COVID-19 patients in Albaha region, Saudi Arabia.

2. Methods

A retrospective cohort study was conducted from 01 April 2020 to 31 August 2020 involving files review of 171 patients admitted to the ICU of a COVID-19 treatment centre in Albaha region as a result of severe symptoms. A list of all COVID-19 patients admitted to the ICU were obtained from the medical administration. Of those patients, 171 patients had a confirmed COVID-19 infection and were included in the study. Patients were confirmed as having the virus by positive SARS-CoV-2 nucleic acid results using a real-time reverse transcriptase-polymerase chain reaction (RT-PCR) assay on nasopharyngeal swab specimens. A data collection form was developed as an Excel file to facilitate the data collection process that was done manually by trained hospital pharmacists that were trained by the investigator on how to collect the data from the hospital electronic medical records system. Demographics, laboratory, clinical, radiological and medications data were collected. Descriptive statistics were used for data analysis. Ethical approval was obtained from the Scientific and Research Committee at the hospital taking part in this study.

Statistical analysis:

The data was expressed as an average value of \pm SD value (standard deviation). Using SPSS software (version 20) to compare variables in the best protocols and co-morbidities, a one-way ANOVA statistical analysis was performed. To analyse categorical data, the χ^2 test was implemented. To detect the relationship between the categorical variables, the Chi-square test was also used in order to compare the clinical features between patients with or without diabetes and with or without hypertension. The length of stay from the date of admission to the discharge/transfer date was recorded for all included patients. The median (IQR) length of stay is presented in tables (3&5). The Kruskal-Wallis analysis was used to compare the medians. *P* values were considered statistically significant if below 0.05.

3. Results

About 32% of the admitted patients for ICU were above 65 years old, 60% males, 45% diabetic, 39% hypertensive, 26% smokers. The patients had symptoms as 79% fever, 78% cough, 75% headache, 59% sore throat and 57% runny nose. More the half of the patients had oxygen saturation less than 90%. About 43% of patients had bilateral infiltration as described in **Table 1**. The most important laboratory findings were 85.4% lymphopenia, 70.8% D-dimer (>0.5

u/ml), 44.4% neutrophilia, and 41% eosinophilia as illustrated in **Table 2**. The length of hospital stay ranged from 4 to 15.6 days and the time in ICU ranged from 4 to 12.7 days as presented in **Table 3**. About 29% of the patients were prescribed antiviral, antimalarial and antibiotics therapy, and unfortunately 35% of those patients died. Around 27.5% of patients were prescribed antibiotics and antimalarial only, of which 13% passed away as shown in **Table 4**. We did not collect data on the factors affecting choice of treatment protocol, but the rationale for choosing triple therapy, the most aggressive protocol, was mainly based on the severity of patients' symptoms and clinicians' attempt, at the time, to kill the virus and reduce the damage it was causing in those severely ill patients. We observed no difference in the mortality rate between the protocol of therapy with or without hydroxychloroquine (P-value: 0.625) as described in **Table 5**. The most prescribed medications were Paracetamol, Ceftriaxone, Azithromycin, Hydroxychloroquine, Enoxaparin, Omeprazole, vitamin D, Zinc, Methylprednisolone, and Dexamethasone as prescribed in **Table 6**.

Table 1: Demographics, symptoms, comorbidities, vital signs and radiological findings

Variables		(n=171)	%
Age	14>	4	2.3%
	15-25	10	5.8%
	26-35	19	11.1%
	36-45	31	18.1%
	46-55	21	12.3%
	56-65	32	18.7%
Gender	66<	54	31.6%
	Male	102	59.6%
Nationality	Female	69	40.4%
	Saudi	127	74.3%
Co-morbidities	Non-Saudi	44	25.7%
	Diabetes mellitus	77	45%
	Hypertension	67	39%
	Pulmonary disease	47	27.4%
	Heart disease	42	24.5%
Smoking	Renal failure	25	14.6%
	Yes	44	25.7%
Symptoms	Fever	135	79%
	Cough	134	78%
	Headache	129	75%
	Sore throat	101	59%
	Runny nose	98	57%
	GI symptoms	81	47%
	Myalgia	57	33%
	Shortness of Breath	53	31%
Vital Signs	Temperature (Cases > 38)	135	79%
	Heart rate: 100 beat/min	55	32%
	Respiratory rate: 24 breath/min	61	35.6%
	Oxygen SAT < 90%	97	56%
Radiological findings upon admission	Bilateral infiltration	74	43%
	Normal	46	27%
	Diffusion reticular opacities	17	10%
	Consolidation	13	7.6%
	Pleural effusion	7	4%

Outcome	Bilateral Pneumonia	6	3.5%
	Linear atelectasis	5	3%
	Cardiomegaly	3	1.7%
	Alive	135	79%
	Death	36	21%

Table 2: Laboratory findings

Lab Test	Normal Value	Abnormal values (n=171)	%
Lymphocytes	0.95-3.07 x 10 ⁽⁹⁾ /L	146	85.4%
D-dimer	< 0.5 µg/ml	121	70.8%
BUN	1.8 – 7.1 mmol/L	79	46.2%
Neutrophils	1.56-6.45 x 10 ⁽⁹⁾ /L	76	44.4%
Eosinophils	0.03-0.48 x 10 ⁽⁹⁾ /L	70	41%
Monocytes	0.26-0.81 x 10 ⁽⁹⁾ /L	69	40.3%
WBC	4.35-5.65 x 10 ⁽¹²⁾ /L	46	26.9%
HB	12-16 g/dL	45	26.3%
ALT	7 – 55 U/L	42	24.6%
PT	11 – 13.5 sec	41	24%
AST	8 – 48 U/L	39	22.8%
ALP	40 – 129 U/L	33	19.3%
Basophils	0.01-0.08 x 10 ⁽⁹⁾ /L	27	15.8
CrCl	≥ 90 ml/min	13	7.6%`
APTT	30 – 45 sec	12	7%

ALP: Alkaline phosphatase, ALT: Alanine transaminase, APTT: Activated partial thromboplastin time, AST: Aspartate transaminase, BUN: Blood urea nitrogen, CrCl: Creatinine Clearance, PT: Prothrombin time, WBC: White blood cells.

Table 3: Length of hospitalization and time in intensive care unit

Age of Patients	Length of hospital stay by day				Time in ICU			
	Mean	SD	Median	IQR	Mean	SD	Median	IQR
<14	4	4	2.5	1.2 - 8.2	4	4	2.5	1.2 – 8.2
15-25	12.3	8.8	11	5.2 - 22	12.2	8.9	11.5	3.7 - 22
26-35	8.3	5.8	7	3 - 14	6.6	4	6	3 - 10
36-45	13.6	12.7	8	6 – 20	10.8	8.3	6	5 - 16
46-55	13.2	8	14	6.5 – 17.5	12.3	7.8	13	5.5 – 16.5
56-65	13.9	9	13	6.2 - 18	12	8.6	11	6 – 14.7
>66	15.6	13.7	12	7 – 18.5	12.7	12	10	6 - 15

Table 4: Distribution of treatment protocol and death among the ICU patients with COVID-19 (n= 171)

Treatment therapy	N (%)	Alive	Died	Died %	P-value
Antiviral+ Antimalarial+ Antibiotics therapy	49(28.7%)	32	17	34.7%	0.001
Antimalarial + Antibiotics therapy	47(27.5%)	41	6	12.8%	0.071
Antibiotics therapy	29(17%)	27	2	6.9%	0.019
Antimalarial therapy	25(14.6%)	22	3	12%	0.140
Antiviral+ Antibiotics therapy	11(6.4%)	8	3	27.3%	0.077
Antiviral+ Antimalarial therapy	7(4.1%)	4	3	42.9%	0.030
Antiviral therapy	3(1.8%)	1	2	66.7%	0.052
Total	171	135	36	21.1%	

Table 5: Comparison of outcomes between G1 and G2.

Outcome	G1 (n=128)				G2 (n=43)				P-value
	Mean	SD	Median	IQR	Mean	SD	Median	IQR	
Time in ICU	11.5	10	9	5 - 15	11	8.4	8	4 - 15	0.625
	N		%		N		%		
Mortality rate	29		22.7%		7		16.3%		0.115

Group 1 (G1): Patient's treatment regimens include Hydroxychloroquine

Group 2 (G2): Patient's treatment regimens DO NOT include Hydroxychloroquine

Table 6: Distribution of medications among ICU COVID-19 patients (n: 171)

Drug Category	Treatment	Frequency	%
Analgesics	Paracetamol	157	91.8%
Prevention of ulcer	Omeprazole	153	89.5%
Anticoagulant	Enoxaparin	141	82.5%
Minerals	Zinc	137	80.1%
Vitamin	Vit. D3	136	79.5%
Anti-malarial	Hydroxychloroquine	104	60.8%
Antibiotics	Ceftriaxone	97	56.7%
	Azithromycin	78	45.6%
Corticosteroids	Methylprednisolone	74	43.3%
	Dexamethasone	50	29.2%
Antiviral	Favipiravir	34	19.9%
	Oseltamivir	13	7.6%
	Lopinavir/Ritonavir	7	4.1%
	Ribavirin	3	1.8%
Antithrombotic	Tinzaparin	6	3.5%
Immunomodulators	Interferon beta – 1B	3	1.8%
Immunosuppressive	Tocilizumab	3	1.8%

4. Discussion

This study explored the the clinical, epidemiological, laboratory, radiological, vital signs and treatment characteristics/outcomes of severe (ICU) COVID-19 patients in Albaha region, Saudi Arabia. We present further evidence to inform healthcare professionals, hospital administrators and public health practitioners of the profile of critically ill COVID-19 patients who are at high risk of admission to ICU.

Age (over 65 years) and male gender remain the most common features among patients admitted to ICU. This has also been reported in a number of Saudi (Alharthy et al., 2021; Alhumaid et al., 2021; Barry et al., 2021) and international studies (Briguglio et al., 2021; Centers for Disease Control and Prevention, 2021; Thomson et al., 2020).

Age alone is a significant factor for severe COVID symptoms (Barry et al., 2021; Centers for Disease Control and Prevention, 2021; Thomson et al., 2020) as it increases the risk of comorbidities, with complex polypharmacy issues and an aging immune system. Furthermore, while male and female patients are both at risk of severe infection requiring ICU admission, male gender has been highlighted as a significant risk factor in many Saudi (Alharthy et al., 2021; Alhumaid et al., 2021) and international studies (Peckham et al., 2020; Thomson et al., 2020). This could be due the high risk of exposure due to socio-economic factors such as working and socializing patterns in a male-dominated society, and the impact of lockdown

measures on the female population (particularly in relation to homeschooling), and the inherent immune differences in male vs, female individuals.

Smoking is another common feature among Saudi ICU patients. Smoking has been suggested to double the risk of severe COVID-19 symptoms (Gülsen et al., 2020), and similar to our study, other studies (Alharthy et al., 2021; Caliskan and Saylan, 2020; Patanavanich and Glantz, 2020) also showed an increased risk of ICU admissions. This could be due to smokers having epithelial cells' damage in the lungs and respiratory comorbidities such as COPD.

Most patients admitted to ICU in our study had diabetes and/ or hypertension. Analysis by (Rawshani et al., 2021) found that type-2 diabetes was independently associated with a higher risk of hospital and ICU admissions and death from COVID-19. The mechanisms behind this are not fully elucidated but it is thought that immunomodulation/ suppression and hyperglycaemia provide a suitable environment for coronavirus to thrive (International Diabetes Federation, 2021). Hypertension in older patients is also associated with severe COVID-19, especially if the patient also has myocardial injury and an established cardiovascular disease (Guo et al., 2020; Williamson et al., 2020). Our findings are similar to reports by (Alharthy et al., 2021; Barry et al., 2021; Richardson et al., 2020; Thomson et al., 2020), where diabetes and/or hypertension were the most common comorbidities for COVID-19 ICU patients.

Lymphopenia (an abnormally low number of blood lymphocytes) is the most common laboratory finding in COVID-19 and is observed in as many as 83 percent of hospitalized patients. Neutrophilia, elevated serum alanine aminotransferase and aspartate aminotransferase levels, elevated lactate dehydrogenase, high CRP and high ferritin levels may be associated with higher disease severity. Elevated D-dimer and lymphopenia were associated with high mortality rate. Procalcitonin is normally common upon entry, but may increase among those admitted to the ICU. Patients with serious illness had elevated plasma levels of inflammatory drugs, indicating possible immune dysregulation (Kermali et al., 2020; Mardani et al., 2020). These presentations have also been reported in other studies (Alharthy et al., 2021; Barry et al., 2021; Casas-Rojo et al., 2020; Gadhiya et al., 2021).

In the severe COVID-19 illness; patients have respiratory frequency >30 breaths per minute, SpO₂ <94 percent at sea level in the room air, ratio of arterial partial oxygen pressure to fraction of inspired oxygen (PaO₂/FiO₂) <300 mmHg, or pulmonary infiltration >50 percent. However, in the critical COVID-19 disease; patients have respiratory failure, septic shock, and/or multiple dysfunctions of the organ. The median time to dyspnea from the onset of disease or symptoms for patients who experienced serious disease ranged from 5 to 8 days, the median time to acute respiratory distress syndrome (ARDS) from the onset of disease or symptoms ranged from 8 to 12 days, and the median time to admission to ICU from the onset of disease or symptoms ranged from 10 to 12 days. Clinicians should be mindful that certain patients have the potential to deteriorate rapidly one week after the onset of the disease (Diamond et al., 2020). Our findings are within the ranges reported in the study by (Alwafi et al., 2021; Rees et al., 2020; Schmidt et al., 2021). The differences observed across countries and regions may be due to the varying local admission and discharge criteria.

Chest radiographs of patients with COVID-19 usually show bilateral air-space consolidation, while patients may have unremarkable chest X-rays at an early stage of the disease. Chest CT images from patients with COVID-19 usually display bilateral, peripheral ground glass opacities. Since this pattern of CT imaging in the chest is non-specific and overlaps with other infections, the diagnostic value of CT imaging in the chest for COVID-19 may be poor and may depend on the radiographic interpretation. One research showed that 56 percent of patients who were diagnosed within two days had normal CT (Jacobi et al., 2020; Rousan et al., 2020).

The treatment protocols for COVID-19 infection in hospital settings have changed dramatically since the onset of the pandemic. The current guidelines suggest a number of antiviral and other medicines including: Favipiravir, Remdesivir, Tocilizumab, prednisolone, dexamethasone, paracetamol etc. (Saudi Ministry of Health, 2021). However, at the start of the pandemic (when this study was carried out), the treatment protocols included a number of antibiotics and antimalarials such as hydroxychloroquine that were suggested at the time to improve outcomes for patients. As evidence continued to emerge, treatment protocols were updated accordingly to reflect the latest evidence (Jomah et al., 2020). We have previously identified no impact of hydroxychloroquine on patients' outcomes (Alghamdi et al., 2021). A systematic review by (Chedid et al., 2021) found that using a cocktail of antibiotics especially earlier on in the pandemic was highly prevalent, despite the lack of efficacy in COVID-19 infections. However, evidence supporting the use of dexamethasone for example resulted in its use to manage covid-19 infections in hospitals across the world (Auwaerter, 2020; Bhimraj et al., 2020).

The evidence for efficacious interventions, once a COVID-19 infected person is admitted to hospital, are still emerging. However, the clinical features and parameters of patients of high risk of infection, admission and staying longer in hospital are starting to strengthen. Our study adds to the current knowledge of patients at risk of developing severe COVID-19 symptoms, and highlights the manifestation of these symptoms to improve resource planning in hospitals treating those patients.

5. Conclusion

The pathogenesis and etiology of COVID-19 remains unknown to date, and targeted therapies for COVID-19 patients are not yet available, with the exception of empirically symptomatic therapies for critically ill patients. Scientists around the world should work together to find successful COVID-19 therapies. Understanding patients' demographics and characteristics of COVID-19 presentation should feed into efforts for disease prevention.

Funding: None

Institutional Review Board Statement: This study was approved by the Scientific and Research Committee at the hospital taking part in this study.

Conflicts of Interest: The author declares no conflict of interest.

References:

- Alghamdi, S., Barakat, B., Berrou, I., Alzahrani, A., Haseeb, A., Hammad, M.A., Anwar, S., Sindi, A.A.A., Almasmoum, H.A., Albanghali, M., 2021. Clinical efficacy of hydroxychloroquine in patients with COVID-19: Findings from an observational comparative study in Saudi Arabia. *Antibiotics* 10, 1–10. <https://doi.org/10.3390/antibiotics10040365>
- Alharthy, A., Aletreby, W., Faqih, F., Balhamar, A., Alaklobi, F., Alanezi, K., Jaganathan, P., Tamim, H., Alqahtani, S.A., Karakitsos, D., Memish, Z.A., 2021. Clinical characteristics and predictors of 28-day mortality in 352 critically ill patients with COVID-19: A retrospective study. *J. Epidemiol. Glob. Health* 11, 98–104. <https://doi.org/10.2991/JEGH.K.200928.001>
- Alhumaid, S., Al Mutair, A., Al Alawi, Z., Al Salman, K., Al Dossary, N., Omar, A., Alismail, M., Al Ghazal, A.M., Jubarah, M.B., Al Shaikh, H., Al Mahdi, M.M., Alsabati, S.Y., Philip, D.K., Alyousef, M.Y., Al Brahim, A.H., Al Athan, M.S., Alomran, S.A., Ahmed, H.S., Al-Shammari, H., Elhazmi, A., Rabaan, A.A., Al-Tawfiq, J.A., Al-Omari, A., 2021. Clinical features and prognostic factors of intensive and non-intensive 1014 COVID-19 patients: an experience cohort from Alahsa, Saudi Arabia. *Eur. J. Med. Res.* 26, 1–13. <https://doi.org/10.1186/s40001-021-00517-7>
- Alsofayan, Y.M., Althunayyan, S.M., Khan, A.A., Hakawi, A.M., Assiri, A.M., 2020. Clinical characteristics of COVID-19 in Saudi Arabia: A national retrospective study. *J. Infect. Public Health* 13, 920–925. <https://doi.org/10.1016/j.jiph.2020.05.026>
- Alwafi, H., Naser, A.Y., Qanash, S., Brinji, A.S., Ghazawi, M.A., Alotaibi, B., Alghamdi, A., Alrhmani, A., Fatehaldin, R., Alelyani, A., Basfar, A., Albarakati, A., Alsharif, G.F., Obaid, E.F., Shabrawishi, M., 2021. Predictors of length of hospital stay, mortality, and outcomes among hospitalised COVID-19 patients in Saudi Arabia: A cross-sectional study. *J. Multidiscip. Healthc.* 14, 839–852. <https://doi.org/10.2147/JMDH.S304788>
- Alyami, M.H., Naser, A.Y., Orabi, M.A.A., Alwafi, H., Alyami, H.S., 2020. Epidemiology of COVID-19 in the Kingdom of Saudi Arabia: An Ecological Study. *Front. Public Heal.* 8, 1–9. <https://doi.org/10.3389/fpubh.2020.00506>
- Arentz, M., Yim, E., Klaff, L., Lokhandwala, S., Riedo, F.X., Chong, M., Lee, M., 2020. Characteristics and Outcomes of 21 Critically Ill Patients With COVID-19 in Washington State. *J. Am. Med. Assoc.* 323, 1612–1614. <https://doi.org/10.1001/jama.2020.4326>
- Auwaerter, P.G., 2020. Coronavirus COVID-19 (SARS-CoV-2) [WWW Document]. Johns Hopkins Med. URL [https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540747/all/Coronavirus_COVID_19_SARS_CoV_2_\(accessed_2.1.21\)](https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540747/all/Coronavirus_COVID_19_SARS_CoV_2_(accessed_2.1.21))
- Barry, M., Althabit, N., Akkielah, L., AlMohaya, A.E., Alotaibi, M., Alhasani, S., Aldrees, A., AlRajhi, A., AlHiji, A., Almajid, F., AlSharidi, A., Al-Shahrani, F.S., Alotaibi, N.H., AlHetheel, A., 2021. Clinical characteristics and outcomes of hospitalized COVID-19 patients in a MERS-CoV referral hospital during the peak of the pandemic. *Int. J. Infect. Dis.* 106, 43–51. <https://doi.org/10.1016/j.ijid.2021.03.058>
- Bhimraj, A., Morgan, R.L., Shumaker, A.H., Laverigne, V., Baden, L., Cheng, V.C.C., Edwards, K.M., Gandhi, R., Muller, W.J., O'Horo, J.C., Shoham, S., Murad, M.H., Mustafa, R.A., Sultan, S., Falck-Ytter, Y., 2020. Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with Coronavirus Disease 2019 (COVID-19). *Clin. Infect. Dis.* 1–20. <https://doi.org/10.1093/cid/ciaa478>
- Briguglio, M., Crespi, T., Pino, F., Mazzocchi, M., Porta, M., De Vecchi, E., Banfi, G., Perazzo, P., 2021. Clinical Characteristics of Severe COVID-19 Patients Admitted to an Intensive Care Unit in Lombardy During the Italian Pandemic. *Front. Med.* <https://doi.org/10.3389/fmed.2021.582896>

- Caliskan, T., Saylan, B., 2020. Smoking and comorbidities are associated with COVID-19 severity and mortality in 565 patients treated in Turkey: A retrospective observational study. *Rev. Assoc. Med. Bras.* 66, 1679–1684. <https://doi.org/10.1590/1806-9282.66.12.1679>
- Casas-Rojo, J.M., Anton-Santos, J.M., Millan-Nunez-Cortes, J., Lumbreras-Bermejo, C., Ramos-Rincon, J.M., Roy-Vallejo, E., Artero-Mora, A., Arnalich-Fernandez, F., Garcia-Brunen, J.M., Vargas-Nunez, J.A., Freire-Castro, S.J., Manzano-Espinosa, L., Perales-Fraile, I., Crestelo-Vieitez, A., Puchades-Gimeno, F., Rodilla-Sala, E., Solis-Marquinez, M.N., Bonet-Tur, D., Fidalgo-Moreno, M.P., Fonseca-Aizpuru, E.M., Carrasco-Sanchez, F.J., Rabadan-Pejenaute, E., Rubio-Rivas, M., Torres-Pena, J.D., Gomez-Huelgas, R., 2020. Clinical characteristics of patients hospitalized with COVID-19 in Spain : results from the SEMI-COVID-19 Registry. *Rev. Clínica Española* 220. <https://doi.org/doi:10.1016/j.rceng.2020.07.003>
- Centers for Disease Control and Prevention, 2021. COVID-19: People at increased risk-Older Adults [WWW Document]. URL <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/older-adults.html> (accessed 7.1.21).
- Chedid, M., Waked, R., Haddad, E., Chetata, N., Saliba, G., Choucair, J., 2021. Antibiotics in treatment of COVID-19 complications: a review of frequency, indications, and efficacy. *J. Infect. Public Health* 14, 570–576. <https://doi.org/10.1016/j.jiph.2021.02.001>
- Chen, T., Wu, D., Chen, H., Yan, W., Yang, D., Chen, G., Ma, K., Xu, D., Yu, H., Wang, H., Wang, T., Guo, W., Chen, J., Ding, C., Zhang, X., Huang, J., Han, M., Li, S., Luo, X., Zhao, J., Ning, Q., 2020. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: Retrospective study. *BMJ* 368. <https://doi.org/10.1136/bmj.m1091>
- Diamond, M., Feliciano, H.L.P., Sanghavi, D., Mahapatra, S., 2020. Acute Respiratory Distress Syndrome. *StatPearls [Internet]*, Treasure Island (FL).
- Gadhiya, K.P., Hansrivijit, P., Gangireddy, M., Goldman, J.D., 2021. Clinical characteristics of hospitalised patients with COVID-19 and the impact on mortality: A single-network, retrospective cohort study from Pennsylvania state. *BMJ Open* 11, 1–13. <https://doi.org/10.1136/bmjopen-2020-042549>
- General Authority for Statistics, 2019. Chapter 01 | Population & Demography [WWW Document]. URL <https://www.stats.gov.sa/en/1007-0> (accessed 7.1.21).
- Gülsen, A., Yigitbas, B.A., Uslu, B., Drömann, D., Kilinc, O., 2020. The Effect of Smoking on COVID-19 Symptom Severity: Systematic Review and Meta-Analysis. *Pulm. Med.* 2020. <https://doi.org/10.1155/2020/7590207>
- Guo, T., Fan, Y., Chen, M., Wu, X., Zhang, L., He, T., Wang, H., Wan, J., Wang, X., Lu, Z., 2020. Cardiovascular Implications of Fatal Outcomes of Patients with Coronavirus Disease 2019 (COVID-19). *JAMA Cardiol.* 5, 811–818. <https://doi.org/10.1001/jamacardio.2020.1017>
- Hammad, M.A., Abdo, M.S., Mashaly, A.M., Syed Sulaiman, S.A., Alghamdi, S., Mohamed Noor, D.A., 2019a. The statins effects on HbA1c control among diabetic patients: An umbrella review of systematic reviews and meta-analyses of observational studies and clinical trials. *Diabetes Metab. Syndr. Clin. Res. Rev.* 13, 2557–2564. <https://doi.org/10.1016/j.dsx.2019.07.005>
- Hammad, M.A., Sulaiman, S.A.S., Aziz, N.A., Noor, D.A.M., 2019b. Prescribing statins among patients with type 2 diabetes: The clinical gap between the guidelines and practice. *J. Res. Med. Sci.* 24, 1–6. https://doi.org/10.4103/jrms.JRMS_100_18
- Hammad, M.A., Syed Sulaiman, S.A., Alghamdi, S., Mangi, A.A., Aziz, N.A., Mohamed Noor, D.A., 2020. Statins-related peripheral neuropathy among diabetic patients. *Diabetes Metab. Syndr. Clin. Res. Rev.* 14, 341–346. <https://doi.org/10.1016/j.dsx.2020.04.005>
- Hammad, M.A., Tangiisuran, B., Kharshid, A.M., Abdul-Aziz, N., Hassan, Y., Aziz, N.A.,

- Elsayed, T.M., 2017. Drug-drug Interaction-related Uncontrolled Glycemia. *J. Pharm. Bioallied Sci.* 9, 221–228. https://doi.org/10.4103/jpbs.JPBS_26_17
- International Diabetes Federation, 2021. COVID-19 and diabetes [WWW Document]. URL <https://www.idf.org/aboutdiabetes/what-is-diabetes/covid-19-and-diabetes/1-covid-19-and-diabetes.html> (accessed 7.1.21).
- Jacobi, A., Chung, M., Bernheim, A., Eber, C., 2020. Portable chest X-ray in coronavirus disease-19 (COVID-19): A pictorial review. *Clin. Imaging* 64, 35–42. <https://doi.org/10.1016/j.clinimag.2020.04.001>
- Jomah, S., Asdaq, S.M.B., Al-Yamani, M.J., 2020. Clinical efficacy of antivirals against novel coronavirus (COVID-19): A review. *J. Infect. Public Health* 13, 1187–1195. <https://doi.org/10.1016/j.jiph.2020.07.013>
- Kermali, M., Khalsa, R.K., Pillai, K., Ismail, Z., Harky, A., 2020. The role of biomarkers in diagnosis of COVID-19 – A systematic review. *Life Sci.* 254. <https://doi.org/10.1016/j.lfs.2020.117788>
- Mangi, A.A., Hammad, M.A., Khan, H., Arain, S.P., Shahzad, M.A., Dar, E., Alam, A., Hassanein, A.H.A., 2020. Evaluation of the geriatric patients prescription for inappropriate medications frequency at Larkana Sindh Hospital in Pakistan. *Clin. Epidemiol. Glob. Heal.* 8, 1390–1394. <https://doi.org/10.1016/j.cegh.2020.06.001>
- Mardani, R., Vasmehjani, A.A., Zali, F., Gholami, A., Mousavi Nasab, S.D., Kaghazian, H., Kaviani, M., Ahmadi, N., 2020. Laboratory Parameters in Detection of COVID-19 Patients with Positive RT-PCR; a Diagnostic Accuracy Study. *Arch. Acad. Emerg. Med.* 8, 4–8. <https://doi.org/10.22037/aaem.v8i1.632>
- Patanavanich, R., Glantz, S.A., 2020. Smoking is associated with COVID-19 progression: A meta-analysis. *Nicotine Tob. Res.* 22, 1653–1656. <https://doi.org/10.1093/ntr/ntaa082>
- Peckham, H., de Gruijter, N.M., Raine, C., Radziszewska, A., Ciurtin, C., Wedderburn, L.R., Rosser, E.C., Webb, K., Deakin, C.T., 2020. Male sex identified by global COVID-19 meta-analysis as a risk factor for death and ICU admission. *Nat. Commun.* 11, 1–10. <https://doi.org/10.1038/s41467-020-19741-6>
- Rawshani, Aidin, Kjölhede, E.A., Rawshani, Araz, Sattar, N., Eeg-Olofsson, K., Adiels, M., Ludvigsson, J., Lindh, M., Gisslén, M., Hagberg, E., Lappas, G., Eliasson, B., Rosengren, A., 2021. Severe COVID-19 in people with type 1 and type 2 diabetes in Sweden: A nationwide retrospective cohort study. *Lancet Reg. Heal. - Eur.* 4, 100105. <https://doi.org/10.1016/j.lanepe.2021.100105>
- Rees, E.M., Nightingale, E.S., Jafari, Y., Waterlow, N.R., Clifford, S., Carl, C.A., Group, C.W., Jombart, T., Procter, S.R., Knight, G.M., 2020. COVID-19 length of hospital stay: A systematic review and data synthesis. *BMC Med.* 18. <https://doi.org/10.1186/s12916-020-01726-3>
- Richardson, S., Hirsch, J.S., Narasimhan, M., Crawford, J.M., McGinn, T., Davidson, K.W., Barnaby, D.P., Becker, L.B., Chelico, J.D., Cohen, S.L., Cockington, J., Coppa, K., Diefenbach, M.A., Dominello, A.J., Duer-Hefe, J., Falzon, L., Gitlin, J., Hajizadeh, N., Harvin, T.G., Hirschwerk, D.A., Kim, E.J., Kozel, Z.M., Marrast, L.M., Mogavero, J.N., Osorio, G.A., Qiu, M., Zanos, T.P., 2020. Presenting Characteristics, Comorbidities, and Outcomes among 5700 Patients Hospitalized with COVID-19 in the New York City Area. *JAMA - J. Am. Med. Assoc.* 323, 2052–2059. <https://doi.org/10.1001/jama.2020.6775>
- Rousan, L.A., Elobeid, E., Karrar, M., Khader, Y., 2020. Chest x-ray findings and temporal lung changes in patients with COVID-19 pneumonia. *BMC Pulm. Med.* 20, 1–9. <https://doi.org/10.1186/s12890-020-01286-5>
- Saudi Ministry of Health, 2021. Saudi MoH Protocol for Patients Suspected of/Confirmed with COVID-19 [WWW Document]. URL <https://www.moh.gov.sa/Ministry/MediaCenter/Publications/Documents/MOH-therapeutic-protocol-for-COVID-19.pdf> (accessed 7.2.21).

- Saudi Ministry of Health, 2020. MOH Reports First Case of Coronavirus Infection [WWW Document]. Saudi Minist. Heal. URL <https://www.moh.gov.sa/en/Ministry/MediaCenter/News/Pages/News-2020-03-02-002.aspx> (accessed 1.27.21).
- Schmidt, M., Hajage, D., Demoule, A., Pham, T., Combes, A., Dres, M., Lebbah, S., Kimmoun, A., Mercat, A., Beduneau, G., Palmyre, J., Prevost, M., Asfar, P., Beloncle, F., Demiselle, J., Pavot, A., Monnet, X., Richard, C., Mayaux, J., Beurton, A., Descamps, R., Joret, A., Du Cheyron, D., Pene, F., Chiche, J.D., Jozwiak, M., Jaubert, P., Voiriot, G., Fartoukh, M., Teulier, M., Blayau, C., L'Her, E., Aubron, C., Bodenes, L., Ferriere, N., Auchabie, J., Le Meur, A., Pignal, S., Mazzoni, T., Quenot, J.P., Andreu, P., Roudau, J.B., Labruyère, M., Nseir, S., Preau, S., Poissy, J., Mathieu, D., Benhamida, S., Paulet, R., Roucaud, N., Thyrault, M., Daviet, F., Hraiech, S., Parzy, G., Sylvestre, A., Jochmans, S., Bouilland, A.L., Monchi, M., Danguy des Déserts, M., Mathais, Q., Rager, G., Pasquier, P., Jean, R., Amélie, S., Charlotte, G., Emmanuel, C., Dellamonica, J., Saccheri, C., Lombardi, R., Kouchit, Y., Jacquier, S., Mathonnet, A., Nay, M.A., Runge, I., Martino, F., Flurin, L., Rolle, A., Carles, M., Coudroy, R., Thille, A.W., Frat, J.P., Rodriguez, M., Beuret, P., Tientcheu, A., Vincent, A., Michelin, F., Melone, M.A., Gauzi, M., Guilbert, A., Kouadri, G., Gissot, V., Ehrmann, S., Salmon-Gandonnière, C., Elaroussi, D., Delbove, A., Fedun, Y., Huntzinger, J., Lebas, E., Kisoka, G., Grégoire, C., Marchetta, S., Lambermont, B., Argaud, L., Baudry, T., Bertrand, P.J., Dargent, A., Guitton, C., Chudeau, N., Landais, M., Darreau, C., Ferre, A., Gros, A., Lacave, G., Bruneel, F., Neuville, M., Devaquet, J., Tachon, G., Gallot, R., Chelha, R., Galbois, A., Jallot, A., Lemoine, L.C., Kuteifan, K., Pointurier, V., Jandeaux, L.M., Mootien, J., Damoiseil, C., Sztrymf, B., Chommeloux, J., Luyt, C.E., Schortgen, F., Rusel, L., Jung, C., Gobert, F., Vimpere, D., Lamhaut, L., Sauneuf, B., Charrier, L., Calus, J., Desmeules, I., Painvin, B., Tadie, J.M., Castelain, V., Michard, B., Herbrecht, J.E., Baldacini, M., Weiss, N., Demeret, S., Marois, C., Rohaut, B., Moury, P.H., Savida, A.C., Couadau, E., Série, M., Alexandru, N., Bruel, C., Fontaine, C., Garrigou, S., Mahler, J.C., Leclerc, M., Ramakers, M., Garçon, P., Massou, N., Van Vong, L.P., Sen, J., Lucas, N., Chemouni, F., Stoclin, A., Avenel, A., Faure, H., Gentilhomme, A., Ricome, S., Abraham, P., Monard, C., Textoris, J., Rimmele, T., Montini, F., Lejour, G., Lazard, T., Etienne, I., Kerroumi, Y., Claire, D., Coupez, B.M., François, T., Hoffmann, C., Donat, N., Muller, V., Martinez, T., Jacquot, A., Mattei, M., Levy, B., Ravan, R., Dopeux, L., Liteaudon, J.M., Roux, Delphine, Rey, B., Anghel, R., Schenese, D., Gevrey, V., Castanera, J., Petua, P., Madeux, B., Hartman, O., Piagnerelli, M., Joosten, A., Noel, C., Biston, P., Noel, T., Bouar, G.L.E., Boukhanza, M., Demarest, E., Bajolet, M.F., Charrier, N., Quenet, A., Zylberfajn, C., Dufour, N., Mégarbane, B., Voicu, S., Deye, N., Malissin, I., Legay, F., Debarre, M., Barbarot, N., Fillatre, P., Delord, B., Laterrade, T., Saghi, T., Pujol, W., Cungi, P.J., Esnault, P., Cardinale, M., Hong Tuan Ha, V., Fleury, G., Brou, M.A., Zafimahazo, D., Tran-Van, D., Avargues, P., Carencio, L., Robin, N., Ouali, A., Houdou, L., Le Terrier, C., Suh, N., Primmaz, S., Pugin, J., Weiss, E., Gauss, T., Moyer, J.D., Paugam-Burtz, C., La Combe, B., Smonig, R., Violleau, J., Cailliez, P., Chelly, J., Marchalot, A., Saladin, C., Bigot, C., Fayolle, P.M., Fatséas, J., Ibrahim, A., Resiere, D., Hage, R., Cholet, C., Cantier, M., Trouiller, P., Montravers, P., Lortat-Jacob, B., Tanaka, S., Tran-Dinh, A., Duranteau, J., Harrois, A., Dubreuil, G., Werner, M., Godier, A., Hamada, S., Zlotnik, D., Nougue, H., Mekontso-Dessap, A., Carteaux, G., Razazi, K., De Prost, N., Mongardon, N., Langeron, O., Levesque, E., Attias, A., de Roquetaillade, C., Chousterman, B.G., Mebazaa, A., Gayat, E., Garnier, M., Pardo, E., Satre-Buisson, L., Gutton, C., Yvin, E., Marcault, C., Azoulay, E., Darmon, M., Bonnet, N., Ebstein, N., Gaudry, S., Cohen, Y., Ait-Oufella, H., Hariri, G., Urbina, T., Mazerand, S., Heming, N., Santi, F., Moine, P., Annane, D., Bouglé, A., Omar, E., Lancelot, A., Begot, E., Plantefeve, G., Contou, D., Mentec, H., Pajot, O., Faguer, S.,

- Cointault, O., Lavayssiere, L., Nogier, M.B., Jamme, M., Pichereau, C., Hayon, J., Outin, H., Dépret, F., Coutrot, M., Chaussard, M., Guillemet, L., Goffin, P., Thouny, R., Guntz, J., Jadot, L., Persichini, R., Jean-Michel, V., Georges, H., Caulier, T., Pradel, G., Hausermann, M.H., Nguyen-Valat, T.M.H., Boudinaud, M., Vivier, E., Rosseli, S., Bourdin, G., Pommier, C., Vinclair, M., Poignant, S., Mons, S., Bougouin, W., Bruna, F., Maestraggi, Q., Roth, C., Bitker, L., Dhelft, F., Bonnet-Chateau, J., Filippelli, M., Morichau-Beauchant, T., Thierry, S., Le Roy, C., Saint Jouan, M., Goncalves, B., Mazeraud, A., Daniel, M., Sharshar, T., Cadoz, C., Gaci, R., Gette, S., Louis, G., Sacleux, S.C., Ordan, M.A., Cravoisy, A., Conrad, M., Courte, G., Gibot, S., Benzidi, Y., Casella, C., Serpin, L., Setti, J. Lou, Besse, M.C., Bourreau, A., Pillot, J., Rivera, C., Vinclair, C., Robaux, M.A., Achino, C., Delignette, M.C., Mazard, T., Aubrun, F., Bouchet, B., Frérou, A., Muller, L., Quentin, C., Degoul, S., Stihle, X., Sumian, C., Bergero, N., Lanaspres, B., Quintard, H., Maiziere, E.M., Egreteau, P.Y., Leloup, G., Berteau, F., Cottrel, M., Bouteloup, M., Jeannot, M., Blanc, Q., Saison, J., Geneau, I., Grenot, R., Ouchike, A., Hazera, P., Masse, A.L., Demiri, S., Vezinet, C., Baron, E., Benchetrit, D., Monsel, A., Trebbia, G., Schaack, E., Lepecq, R., Bobet, M., Vinsonneau, C., Dekeyser, T., Delforge, Q., Rahmani, I., Vivet, B., Paillot, J., Hierle, L., Chaignat, C., Valette, S., Her, B., Brunet, J., Page, M., Boiste, F., Collin, A., Bavoze, F., Garin, A., Dlala, M., Mhamdi, K., Beilouny, B., Lavalard, A., Perez, S., Veber, B., Guitard, P.G., Gouin, P., Lamacz, A., Plouvier, F., Delaborde, B.P., Kherchache, A., Chaalal, A., Ricard, J.D., Amouretti, M., Freitas-Ramos, S., Roux, Damien, Constantin, J.M., Assefi, M., Lecore, M., Selves, A., Prevost, F., Lamer, C., Shi, R., Knani, L., Pili-Floury, S., Vettoretti, L., Levy, M., Marsac, L., Dager, S., Guilmin-Crépon, S., Putegnât, J.B., Bayle, F., Perrou, M., Thao, G., Géri, G., Charron, C., Repessé, X., Vieillard-Baron, A., Guilbart, M., Roger, P.A., Hinard, S., Macq, P.Y., Chaulier, K., Goutte, S., Chillet, P., Pitta, A., Darjent, B., Bruneau, A., Lasocki, S., Leger, M., Gergaud, S., Lemarie, P., Terzi, N., Schwebel, C., Dartevél, A., Galerneau, L.M., Diehl, J.L., Hauw-Berlemont, C., Péron, N., Guérot, E., Amoli, A.M., Benhamou, M., Deyme, J.P., Andremont, O., Lena, D., Cady, J., Causeret, A., De La Chapelle, A., Cracco, C., Rouleau, S., Schnell, D., Lory, C., Chapelle, T., Bruckert, V., Garcia, J., Sahraoui, A., Abbosh, N., Bornstain, C., Pernet, P., Poirson, F., Pasem, A., Karoubi, P., Poupinel, V., Gauthier, C., Bouniol, F., Feuchere, P., Bavoze, F., Heron, A., Carreira, S., Emery, M., Le Floch, A., Giovannangeli, L., Herzog, N., Giacardi, C., Baudic, T., Thill, C., Tubach, F., Lesieur, O., Noublanche, J., 2021. Clinical characteristics and day-90 outcomes of 4244 critically ill adults with COVID-19: a prospective cohort study. *Intensive Care Med.* 47, 60–73. <https://doi.org/10.1007/s00134-020-06294-x>
- Shabrawishi, M., Al-Gethamy, M.M., Naser, A.Y., Ghazawi, M.A., Alsharif, G.F., Obaid, E.F., Melebari, H.A., Alamri, D.M., Brinji, A.S., AlJehani, F.H., Almaini, W., Ekram, R.A., Alkhatib, K.H., Alwafi, H., 2020. Clinical, radiological and therapeutic characteristics of patients with COVID-19 in Saudi Arabia. *PLoS One* 15, 1–11. <https://doi.org/10.1371/journal.pone.0237130>
- Thomson, R.J., Hunter, J., Dutton, J., Schneider, J., Khosravi, M., Casement, A., Dhadwal, K., Martin, D., 2020. Clinical characteristics and outcomes of critically ill patients with COVID-19 admitted to an intensive care unit in London: A prospective observational cohort study. *PLoS One* 15, 1–16. <https://doi.org/10.1371/journal.pone.0243710>
- Williamson, E., Walker, A.J., Bhaskaran, K., Bacon, S., Bates, C., Morton, C.E., Curtis, H.J., Mehrkar, A., Evans, D., Inglesby, P., Cockburn, J., McDonald, H.I., Mackenna, B., Douglas, I.J., Rentsch, C.T., Mathur, R., Wong, A., Harrison, D., Forbes, H., Schultze, A., Croker, R., Parry, J., Harper, S., Perera, R., Evans, S., Smeeth, L., Goldacre, B., 2020. OpenSAFELY: factors associated with COVID-19-related hospital death in the linked electronic health records of 17 million adult NHS patients. *medRxiv Prepr.* 0–21. <https://doi.org/10.1101/2020.05.06.20092999>

World Health Organization, 2020. WHO Timeline - COVID-19 [WWW Document]. World Heal. Organ. URL <https://www.who.int/news/item/27-04-2020-who-timeline---covid-19> (accessed 1.28.21).

Clinical characteristics and treatment outcomes of severe (ICU) COVID-19 patients in Saudi Arabia: A single centre study

Saleh Alghamdi^{1*}

¹Department of Clinical Pharmacy, Faculty of clinical Pharmacy, Albaha University, Albaha, Saudi Arabia

* Correspondence: saleh.alghamdi@bu.edu.sa